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The year 2017 in cardiology: aorta and peripheral circulation

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Preamble

More than 83 million people live with cardiovascular (CV) disease in the ESC member countries, with peripheral vascular diseases as the most predominant condition (more than 35 million) followed by ischaemic heart disease (>29 million), underlining the public health burden of the former in our continent.¹

The ESC collaborated with European Society of Vascular Surgery (ESVS) to publish the most comprehensive guidelines document on the management of peripheral arterial diseases (PADs), encompassing all the peripheral territories.² Compared to the 2011 version, major changes regard risk stratification for patients with asymptomatic carotid disease, and those with critical limb-threatening ischaemia (CLTI), and a new specific chapter on cardiac diseases in patients with PADs. Any presentation of PADs is associated with a very high risk for CV events, and all patients require best medical therapy for secondary prevention. In this respect, the VIVA³ and COMPASS⁴ trials are definitely the two seminal randomized controlled trials (RCTs) of the year.

The VIVA trial demonstrated the interest of multiple vascular screening to improve population longevity (Table 1).³ Over 50 000 Danish men were randomized to receive an invitation for vascular screening or not. Vascular screening consisted of arm blood pressure and ankle-brachial index (ABI) measurement, and abdominal aorta ultrasound. Positive cases were invited to consult their general practitioners, while large abdominal aorta aneurysm (AAA) were referred to vascular surgeons. After 4.4 years, the mortality was significantly lower in the screening group (Table 1). The number needed to screen to prevent one death was 169, far below the one necessary for any cancer screening.

The COMPASS trial randomized 27 395 patients either with coronary artery disease (CAD) or PADs [lower-extremity artery disease

(LEAD) or carotid stenosis or prior carotid revascularization] to three different antithrombotic strategies. In the pre-defined sub-analysis of patients with PADs, the results were consistent with those obtained in the entire population (Table 1): the combination of rivaroxaban 2.5 mg b.i.d. + aspirin 100 mg was associated with a significant 28% reduction of a combination of CV death, myocardial infarction, or stroke and a 46% reduction of major adverse limb events (MALE), including amputation, as compared to aspirin 100 mg.⁴ Bleeding events were higher under the combination therapy, except for fatal bleeding. The net benefit including ischaemic and major bleeding events remained in favour of the combination strategy. The clinical implication for the management of these patients needs further analyses to select specific subgroups with an optimal benefit/risk ratio (RR). Also, the external applicability of these results is important; among REACH participants with LEAD, 68% were COMPASS-compatible, fulfilling inclusion, and exclusion criteria.¹⁵ The main reason for not being COMPASS-compatible was a high-bleeding risk. Hence, the bleeding risk stratification is of paramount importance.

Other specific studies in lower-extremity artery disease

The 2017 ESC guidelines¹ emphasize the optimal management of risk factors in patients with PADs. A new analysis of the FOURIER trial underscored the importance of lowering LDL-cholesterol in patients with LEAD, with significant benefits with evolocumab, a PCSK-9 inhibitor (Table 1).⁷ This new analysis in patients with LEAD showed similar benefits in terms of CV events reduction, and a significant reduction of MALE. This is the first trial showing the benefits of a lipid-lowering drug to reduce MALE, including amputation.

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Table 1 Summary of major randomized trials in peripheral intervention in 2017

Trial's acronym (or first author)	Type and aim of the study	Challenger (n)	Reference (n)	Setting (indication)	Primary outcome (+ secondary outcomes of interest)
Multiple localization COMPASS-PAD ⁴	Double-blind: interest of low-dose rivaroxaban (alone or with aspirin) in patients with PADs	Rivaroxaban 2.5 mg x 2 + Aspirin 100 mg (R + A: 2492) or Riva 5 mg x 2 (R: 2474)	Aspirin 100 mg (A: 2504)	LEAD (past revascularization, claudication with proven LEAD, or CAD with ABI < 0.90) or carotid disease (past revascularization or carotid stenosis > 50%)	CV death, MI or Stroke: R+A vs. A = -28% (P=0.0047); R vs. A = -14% (P=0.19). -46% reduction of MALE for R + A vs. A. +61% bleeding risk, but not fatal bleeding.
VIVA ³	Open: interest of vascular screening in general population	Screening for hypertension, LEAD and AAA (25 078)	No screening (25 078)	Men aged 65–74 years in Central Denmark	Mortality (HR 0.93; 95% CI 0.88–0.98)
Carotid artery disease Moresoli ⁵	Meta-analysis: CAS versus CEA in patients with asymptomatic carotid stenosis	CAS (1881)	CEA (1138)	Asymptomatic carotid stenosis	Any peri-procedural stroke and long-term stroke (RR 1.24; 95% CI 0.76–2.03) or death (RR 1.72; 95% CI 0.95–3.11)
Lower extremities artery disease EMPA-REG (LEAD subgroup) ⁶	Double-blind: efficacy and safety of empagliflozin on top of standard care in type 2 diabetic patients with LEAD	Empagliflozin (982)	Placebo (479)	LEAD (past revascularization or amputation, stenosis > 50%, or ABI < 0.90)	CV death: HR, 0.57; 95% CI, 0.37–0.88. -38% all-cause mortality reduction No increased risk of amputation.
FOURIER (LEAD subgroup) ⁷	Double-blind: interest of evolocumab on top of statins to reduce cardiovascular events	Evolocumab (1856)	Placebo (1780)	Claudication and ABI < 0.85 or prior revascularization	Composite: CV death, MI, stroke, hospitalization for unstable angina, or coronary revascularization: -21% (P < 0.01). MALE also reduced by -42% (P < 0.01)
ICE ⁸	Open: SES vs. BES for iliac occlusive disease	SES (340)	BES (320)	Moderate to severe claudication caused by iliac artery stenosis or occlusion	Binary restenosis at 12 months 6.1% (SES) vs. 14.9% (BES) P = 0.006
ISAR-STATH ⁹	Open: endovascular techniques for superficial femoral artery revascularization	DCB + stent (48) or atherectomy (52)	BMS (55)	stenosis or occlusion of superficial femoral artery	(1) Diameter stenosis in percentages measured by angiography 34%. 56% vs. 55%; P = 0.009 and 0.007; (2) Binary restenosis rate 7.23% vs. 22.52% vs. 24.54%; P = 0.0017 PEB + stent vs. BA + stent
ILLUMINATE pivotal ¹⁰	Single-blind: DCB vs. PTA in femoropopliteal disease	DCB (200)	PTA (100)	Rutherford Class 2–4 LEAD caused by femoropopliteal stenosis or occlusion	(1) Composite: 12 months of freedom from device and procedure-related 30 days of death, and from target limb major amputation and CD-TLR: 92.1% vs. 83.2% P = 0.001; (2) 12 months ^a primary patency 76.3% vs. 57.6% P = 0.003

Continued

Table 1 Continued

Trial's acronym (or first author)	Type and aim of the study	Challenger (n)	Reference (n)	Setting (indication)	Primary outcome (+ secondary out- comes of interest)
ILLUMENATE EU ¹¹	Single-blind: DCB vs. PTA in femoro-popliteal disease	DCB (222)	PTA (72)	Moderate to severe claudication or ischemic rest pain caused by fem- oro-popliteal stenosis or occlusion	(1) Composite: 30 days of freedom from device- and procedure-related death, and 12 months ^b from target limb major amputation and CD-TLR: 94.1% vs. 83.3%. (2) Primary patency 12 months ^b and freedom from CD-TLR 83.9% vs. 60.6% $P = 0.001$
Venous thrombo-embolic disease EINSTEIN-choice ¹²	Double-blind: Efficacy & safety of two doses of rivaroxaban vs. aspirin in long-term after VTE	Rivaroxaban 10 mg OD (R10: 1127) Rivaroxaban 20 mg OD (R20: 1107)	Aspirin 100 mg OD (A: 1131)	After 6–12 months of anticoagulation for acute DVT or PE	Symptomatic recurrent fatal or nonfatal VTE R20 vs. A: -66% ($P < 0.001$) R10 vs. A: -74% ($P < 0.001$) No significant increase major bleeding risk No significant difference in PTS rates (47% in the pharmacomechanical-thrombolysis group vs. 48% in the control group; $P = 0.56$)
ATTRACT ¹³	Open ^c : efficacy and safety of pharmaco-mechani- cal thrombolysis to prevent PTS after prox- imal DVT	Pharmaco-mechanical thromboly- sis + anticoagulation (337)	Anticoagulation (355)	Post-thrombotic syndrome between 6 and 24 months	
PETHO (long-term results) ¹⁴	Double-blind: long-term efficacy and safety of thrombolysis for inter- mediate-risk PE	Tenecteplase (506)	Placebo (499)	Intermediate-risk PE < 5 days and RV dysfunction and/or troponin release	Median FU 37 months: No significant difference in terms of mortality, residual dyspnoea, and chronic thrombo- embolic pulmonary hypertension

A, aspirin; AAA, abdominal aorta aneurysm; BES, balloon-expandable stent; CAD, coronary artery disease; CAS, carotid artery stenting; CD, clinically driven; CEA, carotid endarterectomy; CV, cardiovascular; DCB, drug-coated balloon; DES, drug-eluting stent; DVT, deep-vein thrombosis; HR, hazard-ratio; LEAD, lower-extremities artery disease; MALE, major adverse limb events; MI, myocardial infarction; PADs, peripheral arterial diseases; PTA, plain balloon angioplasty; PTS, post-thrombotic syndrome; R, rivaroxaban, R + A, rivaroxaban plus aspirin; RR, relative risk; SES, self-expandable stent; SFA, superficial femoral artery; TLR, target lesion revascularization.

^aDefined as absence of target lesion restenosis, measured by duplex ultrasonography-derived peak systolic velocity ratio ≤ 2.5 and freedom from CD-TLR.

^bDefined as the absence of target lesion restenosis on duplex ultrasound (peak systolic velocity ratio ≤ 2.5).

^cWith blinded assessors.

Many patients with LEAD are diabetic. Recently strikingly positive results on the CV benefits of sodium glucose cotransporter 2-inhibitors have been presented, although concerns were raised regarding the increased risk of amputation (mostly minor) with canagliflozin.¹⁶ A new analysis of patients with LEAD enrolled in the EMPA-REG trial confirmed the benefits of empagliflozin in terms of mortality and CV events (Table 1), without any difference in amputation rates as compared to placebo.⁶ The need for improved diabetes care was underlined by a recent registry on 15 332 CLTI patients (47% diabetic), showing that in spite of a 60% higher risk of infection and 40% higher amputation rate (both in-hospital and at 4-year follow-up), diabetic patients were revascularized less often (46% vs. 54%, $P < 0.001$).¹⁷

In another review of 60 998 hospitalizations of patients undergoing revascularization or amputation in the USA for CLTI, the 30-days readmission rate was 20%, mainly due to infections, persistent CLTI symptoms, cardiac conditions, and procedural complications.¹⁸

Regarding revascularization, the *Iliac, Common and External Artery Stent Trial* (ICE) is the first RCT to compare balloon-expandable (BES) vs. self-expandable stents (SES).⁸ Among 660 patients undergoing iliac stenting, 1-year binary restenosis was significantly lower after SES as compared to BES (Table 1). Furthermore, freedom from target lesion revascularization (TLR) was higher in the SES group, with no difference in peri-procedural complications or functional outcome. At the femoropopliteal level, new evidence regarding device choice came from a network meta-analysis (6091 patients).¹⁹ Five endovascular strategies were compared: bare metal stent (BMS), covered metal stent (CMS), drug-eluting stent (DES), drug-coated balloon (DCB), and plain balloon angioplasty (PTA). Drug-coated balloon, DES, and CMS offered a significant reduction in 1-year TLR vs. PTA (68%, 58%, and 48%, respectively). Additionally, DCB significantly reduced TLR also vs. BMS (53%), appearing the preferable revascularization device. The advantages of DCB were confirmed in *ISAR-STATH*, an RCT randomizing 155 patients to three different strategies: DCB + BMS, PTA + BMS, or directional atherectomy.⁹ The primary endpoint was significantly lower for DCB + BMS than PTA + BMS, as well as 2-year TLR (Table 1). Further evidence favouring DCB over PTA comes from the *ILLUMINATE pivotal*¹⁰ and *ILLUMINATE EU*¹¹ which randomized 300 and 222 patients, respectively, to DCB or PTA; primary patency was significantly higher for DCB in both trials (Table 1).

Cardiac risk should be assessed in patients undergoing vascular surgery.² In a nationwide US registry of patients undergoing non-cardiac surgery, peri-operative myocardial infarction occurred in 2% of patients with vascular surgery, among the highest risks compared to other types of non-cardiac intervention [odds ratio (OR) 1.56, 95% confidence interval (95% CI) 1.52–1.59].²⁰ Through a propensity-matched analysis, the registry suggests that invasive management of peri-operative myocardial infarction would improve outcomes; this deserves a trial enrolling patients with PADs.

Carotid artery disease

Optimal medical management

Patients with asymptomatic carotid artery stenosis should benefit from best medical therapy.¹ This has recently been confirmed in 864 patients with 50–69% or 70–99% carotid artery stenosis.²¹

Altogether, 4929 carotid ultrasound studies were performed on 1439 carotid arteries over 6.5 years. Ischaemic stroke/transient ischaemic attack (TIA) and carotid revascularization occurred in 12.2% and progression of the stenosis in 21.5% of patients. The quality of risk factors control were independent predictors for the stenosis progression or occurrence of stroke/TIA (Figure 1).²¹

Revascularization

A meta-analysis of five RCTs including 3019 asymptomatic patients compared carotid artery stenting (CAS) to surgery (CEA).⁵ After CAS, the risk of any peri-procedural stroke and non-disabling stroke as well as the composite of any peri-procedural stroke or death was increased with borderline statistical significance (Table 1). There was a trend for less peri-procedural myocardial infarctions after CAS. There was no significant difference regarding incident long-term stroke between the two techniques.

Women are at increased risk of peri-operative stroke, but gender-specific data are sparse. In the National Surgical Quality Improvement Program database (5620 CEA and 141 CAS), the early post-operative outcomes in women with symptomatic carotid artery stenosis were compared. During the first 30 days, MACE occurred in 12.2% and 5.2%, respectively after CAS and CEA ($P < 0.001$).²² In a propensity-matched analysis including 125 pairs, the 30-day incidence of post-operative MACE in the CAS group was 11.2% vs. 4.0% after CEA (OR 2.8; $P = 0.04$). This is in favour of CEA as the preferred option in women.

Early revascularization after an ischaemic stroke/TIA is recommended in case of carotid stenosis, but the influence of the timing on revascularization techniques has been poorly studied. In a pooled analysis of individual data of 4138 patients from four RCTs, the risk of stroke or death after CAS was higher than after CEA in those treated within 7 days (8.3% vs. 1.3%, RR 6.7; 95% CI 2.1–21.9, adjusted for age, sex, and type of qualifying event).²³ These results favour of CEA in the early days after a neurologic ischaemic event.

In a German registry (2009–14), a total of 13 086 CAS procedures were analysed.²⁴ In-hospital stroke or death occurred in 2.4% (1.7% in asymptomatic and 3.7% in symptomatic patients). The multivariable analysis showed the use of an embolic protection device was an independent predictor of lower in-hospital rates of stroke or death (adjusted RR 0.65; 95% CI 0.50–0.85), major stroke or death (adjusted RR 0.60; 95% CI 0.43–0.84), and stroke (adjusted RR 0.57; 95% CI: 0.43–0.77). This supports the recent recommendations in favour of embolic protection device during CAS.²

Current practice of carotid revascularization was evaluated in 12 countries.²⁵ Among 58 607 treated cases, the largest national and international variation was seen in indications: overall, about half of the patients were asymptomatic (48%), but this varied from 0% (Denmark) to 73% (Italy). National variation between centres was even bigger and was the highest in Australia (0–72%), Hungary (5–55%), and the USA (0–100%). The odds for revascularization for asymptomatic carotid stenosis were much higher in countries where fee per case is paid to the operator (OR 5.8, 95% CI 4.4–7.7). Among asymptomatic patients CAS was used most often in Sweden (26%) while some countries (Finland, Iceland) did not use CAS at all. An international effort is necessary to homogenize guidelines and practices globally.

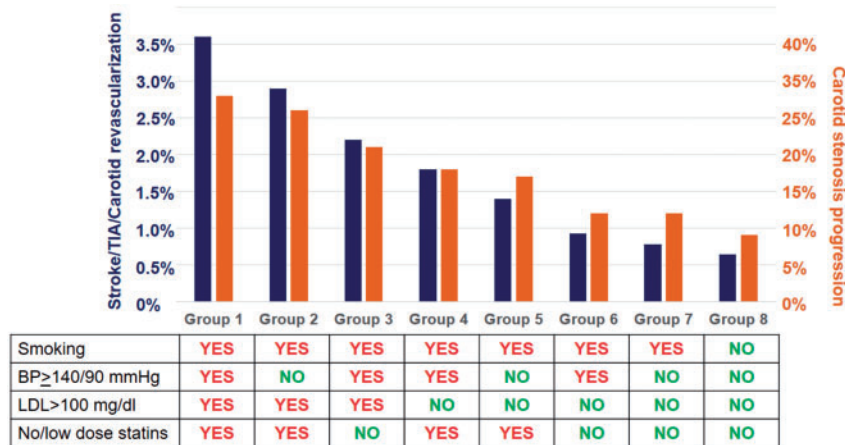


Figure 1 Neurologic ischaemic events and stenosis progression in patients with asymptomatic carotid stenosis according to the quality of risk factors management. Adapted from Shah *et al.*²¹ BP, blood pressure; TIA, transient ischemic attack.

Aorta

Thoracic aorta

Echocardiography remains the most frequent imaging method to assess the proximal aorta. The diameter varies according to the cardiac cycle, site, and mode of measurement as well as age and body size. In the multicentre collaborative NORRE study including more than 700 healthy individuals, the normal reference ranges for the proximal aorta dimensions have been set.²⁶

Two studies from the Multi-Ethnic Study of Atherosclerosis reported on aortic calcification on computed tomography (CT): the first assessed the ascending aorta calcium and showed that this condition is rare in general population (3.4%).²⁷ The ascending aorta calcium density was inversely correlated with CV events, even after adjustments for risk factors and the coronary artery calcium. The second study focused on those with coronary artery calcium score of zero and found no additional prognostic information from ascending aorta calcium.²⁸ A magnetic resonance imaging study showed the prognostic interest of the aortic arch pulse-wave velocity, a marker of aortic stiffness, in middle-age (45–54 years) subjects, but not at older ages.²⁹

Regarding aortic events, so far only the aortic diameter is considered as a risk marker from imaging for aortic dissection. Two independent case-control studies, comparing patients with type-B aortic dissection (TB-AD) with controls, suggest that beyond the diameter, the age-related elongation of the aortic arch is also associated with increased risk of TB-AD.^{30,31}

Abdominal aorta

After screening, small AAAs require follow-up of the diameter, typically assessed by 2D ultrasound (US). Using 3D-US for assessment of AAA volume in 179 patients with small AAAs, it was found that 3D-US was accurate in assessing both diameter and volume as compared to CT.³² During follow-up, 40% patients classified as stable according to the diameter actually presented a volume growth highlighting the higher sensitivity of this new method.

Data from one of the most comprehensive and nationwide registries in Europe come from Finland, showing the improvement in the prognosis of patients with unruptured and ruptured AAA during the last 2 decades (Figure 2).³³ The VascuNet network analysed differences in AAA interventional methods and outcomes in 83 253 patients through 11 countries during the 2005–09 and 2010–13 periods.³⁴ The proportion of octogenarians operated increased between the two periods from 18.5% to 23.1% ($P < 0.0001$) and similarly the proportion of patients treated with endovascular aneurysm repair (EVAR) increased from 44.3% to 60.6% ($P < 0.0001$). Mortality for EVAR decreased from 1.5% to 1.1% ($P < 0.0001$), but the outcome worsened for open repair from 3.9% to 4.4% ($P = 0.008$).

In some countries, AAAs are repaired by EVAR at a lower diameter than recommended in guidelines. Based on data from almost 40 000 Medicare patients undergoing EVAR from 2001 to 2008, earlier AAA repair by 5 mm has major consequences, with 22% excess EVAR procedures and 42% and 37% increase in open and endovascular re-interventions.³⁵ The cost per saved AAA rupture was estimated to be 1 million USD.

After EVAR lifelong surveillance is necessary and CT-angiography has been the preferred modality, while ultrasound duplex scanning (DUS) with and without contrast enhancement (CEUS) is an alternative. A Cochrane review of 42 studies³⁶ concluded that both DUS and CEUS have high specificity for identification of endoleaks; however, CEUS is more sensitive and can be routinely used, with CT scan only when endoleak is suspected.

Venous thromboembolism

After an acute episode of venous thromboembolism (VTE) anticoagulation is indicated for at least 3 months.³⁷ Optimal anticoagulation duration, beyond the initial period remains uncertain. Prandoni *et al.* showed that anticoagulation in patients with a first episode of proximal DVT, based on the assessment of residual vein thrombosis and serial D-dimer, leads to an overall annual rate of recurrent

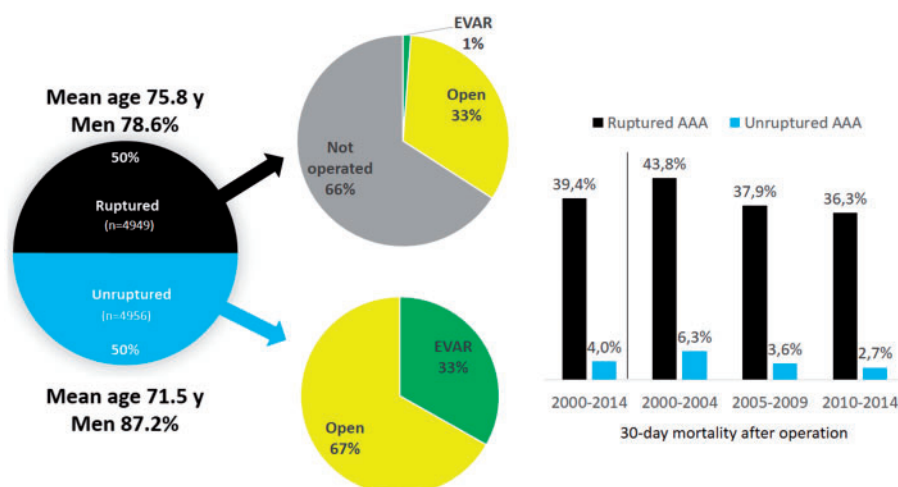


Figure 2 Management of abdominal aorta aneurysm in the nationwide registry in Finland, 2000–14. Adapted from Laine et al.³³ AAA, abdominal aorta aneurysm; EVAR, endovascular aneurysm repair.

Table 2 Characteristics included in the risk prediction scores for cancer-related venous thromboembolism (VTE)

	Khorana	Vienna CATS	PROTECHT	CONKO
Very high-risk tumours (pancreatic or gastric cancer) ^a	2	2	2	2
High-risk tumours (lung, gynaecological, lymphoma, bladder, or testicular cancer)	1	1	1	1
Pre-chemotherapy haemoglobin <10 g/dL or use of erythropoietin stimulating agents	1	1	1	1
Pre-chemotherapy white blood cell count >11 × 10 ⁹ /L	1	1	1	1
Pre-chemotherapy platelet count ≥350 × 10 ⁹ /L	1	1	1	1
Body mass index >35 kg/m ²	1	1	1	
D-dimer >1.44 µg/mL		1		
Soluble P-selectin ≥53.1 ng/mL		1		
World Health Organization (WHO) performance status ≥2				1
Gemcitabine chemotherapy			1	
Platinum-based chemotherapy			1	
Cut-off for classification of high-risk patients (points)	≥3	≥5	≥3	≥3

Numbers represent the value attributed to each characteristic in the scores.

^aThe Vienna CATS also included brain cancer as a high-risk site.

VTE <5%.³⁸ However, in men this strategy needs further assessment. Several prediction rules are proposed to identify patients at high risk of recurrence.³⁹ The REVERSE II study prospectively validated the 'men continue and HERDOO2' clinical prediction rule.⁴⁰ This allows identifying low-risk women, following a first unprovoked VTE, who can safely discontinue anticoagulation once the initial treatment is completed (3.0% recurrence per patient-year in low-risk women). No predictors for low risk of recurrence were found in men. The decision on whether to discontinue anticoagulation should therefore be individually tailored and balanced against bleeding risk.

Once the decision to extend anticoagulant treatment is taken, common agreement is to continue with the initial compound. The latest EINSTEIN-CHOICE trial¹² showed that standard (20 mg o.d.) and lower dose rivaroxaban (10 mg o.d.), significantly reduced the

risk of recurrence compared to aspirin, without significant increase in bleeding rates (Table 1).

In patients with proximal DVT treated with DOACs, persistence of residual vein thrombosis is likely to occur less frequently than in patients treated with conventional anticoagulation. These results may have implications for the prognosis of patients with DVT.⁴¹

According to current guidelines, adjuvant catheter-directed thrombolysis may be considered in selected patients with acute ilio-femoral DVT, if performed in experienced centres, to diminish risk of post-thrombotic syndrome (PTS). However, the recently published ATTRACT trial (692 patients) failed to show the additional interest of catheter-directed thrombolysis to decrease the risk of PTS, but did result in a higher risk of major bleeding.¹³ While the PTS severity score was lower in the pharmacomechanical group, this did not affect

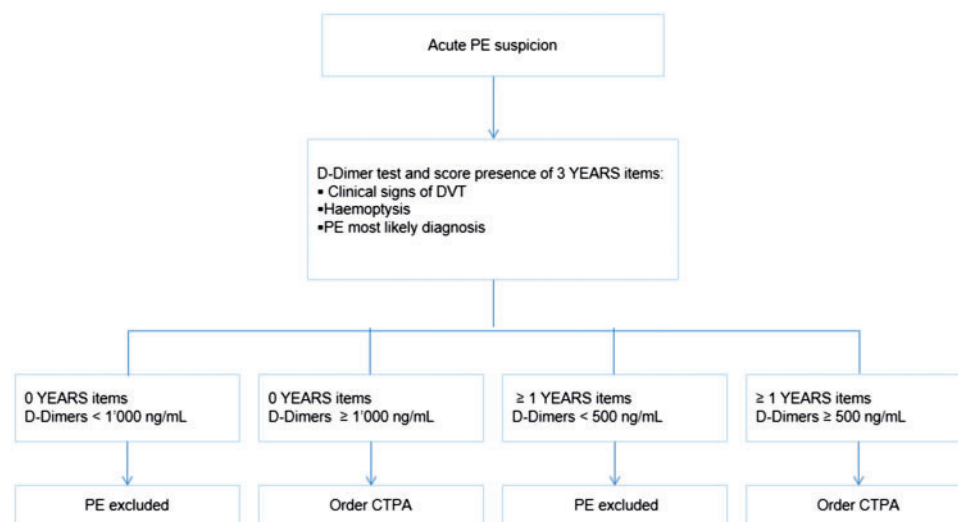


Figure 3 The YEARS diagnostic strategy in case of suspicion for pulmonary embolism. CTPA, computed tomography pulmonary angiography; DVT, deep vein thrombosis; PE, pulmonary embolism.

improve the quality of life of the patients. There was no difference according to the site of DVT (57% had ilio-femoral DVT). The overall results are in contradiction with a smaller trial reported previously in favour of pharmacomechanical intervention, with decreased risk of PTS after 5 years of follow-up.⁴² Further trials, focused on ilio-femoral DVT, are required.

The clinical usefulness of VTE risk prediction scores in ambulatory cancer patients is debated. A cohort of 876 cancer patients compared several scores (Table 2).⁴³ All models performed poorly (c-statistics: 0.50–0.57), indicating the need for improvements before these models can be considered in clinical practice. Identifying predictors for VTE recurrence in cancer patients remains a challenge. In two cohorts of patients with cancer-associated VTE, the modified Ottawa score showed modest discriminating power and was unable to predict the risk of VTE recurrences.^{44,45}

Diagnostic algorithms are frequently used to identify patients in whom pulmonary embolism (PE) can be ruled out without the use of computed tomography pulmonary angiography (CTPA). In a study of 3465 patients with suspected PE, the YEARS decision rule (based on three clinical items combined with two D-dimer cut-offs) yielded a 14% decrease in CTPA examinations compared to conventional strategies (Figure 3) with a negative predictive value of 99.4%.⁴⁶ Whether negative CTPA is sufficient to exclude PE in patients with likely pretest probability is debated. Pulmonary embolism was excluded with CTPA in 37% of patients with likely clinical probability, and the 3-month VTE risk was 0.6%, indicating that a negative CTPA safely excludes PE in this patient group.⁴⁷

The prevalence of PE in patients presenting with syncope has been highly debated this year, following the PESIT trial, reported last year,³⁹ describing a 17% rate of PE in syncope cases referred to emergency rooms, after excluding cases with evident aetiology. A meta-analysis including 6608 emergency department patients and 975 patients hospitalized for syncope reported a PE prevalence <1%.⁴⁸ Two other studies reported a PE prevalence of 1.4% among

patients with syncope.^{14,49} Routine screening for PE in all patients presenting with syncope may not be justified.

The PEITHO trial investigated long-term prognosis in patients with intermediate-risk PE randomized to receive thrombolysis or placebo.⁵⁰ Thrombolytic treatment did not decrease long-term mortality rates, persisting dyspnoea, chronic thromboembolic pulmonary hypertension, or right ventricular dysfunction.

Conflict of interest: V.A.: AstraZeneca, Bayer, Boehringer-Ingelheim, Novartis, Pfizer/BMS Alliance, Sanofi. S.B.: none. L.M.: Bayer, Pfizer/BMS Alliance, Sanofi. H.S.: Amgen, Bayer, Novo Nordisk, B Braun, Philips and Cook Medical. M.V.: Bayer. M. De C.: Daiichi-Sankyo, Abbott Vascular, Philips-Volcano, Sanofi.

References

1. Timmis A, Townsend N, Gale C, Grobbee R, Maniadakis N, Flather M, Wilkins E, Wright L, Vos R, Bax J, Blum M, Pinto F, Vardas P. European Society of Cardiology: Cardiovascular Disease Statistics 2017. *Eur Heart J* 2018;**39**:508–577.
2. Aboyans V, Ricco J-B, Bartelink M-LEL, Björck M, Brodmann M, Cohnert T, Collet J-P, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018;**39**:763–816.
3. Lindholt JS, Sogaard R. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. *Lancet* 2017;**390**: 2256–2265.
4. Anand SS, Bosch J, Eikelboom JW, Connolly SJ, Diaz R, Widimsky P, Aboyans V, Alings M, Kakkar AK, Keltai K, Maggioni AP, Lewis BS, Störk S, Zhu J, Lopez-Jaramillo P, O'donnell M, Commerford PJ, Vinereanu D, Pogosoova N, Ryden L, Fox KAA, Bhatt DL, Misselwitz F, Varigos JD, Vanassche T, Avezum AA, Chen E, Branch K, Leong DP, Bangdiwala SI, Hart RG, Yusuf S; COMPASS Investigators. Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2017; doi:10.1016/S0140-6736(17)32409-1.
5. Moresoli P, Habib B, Reynier P, Secrest MH, Eisenberg MJ, Filion KB. Carotid stenting versus endarterectomy for asymptomatic carotid artery stenosis: a systematic review and meta-analysis. *Stroke* 2017;**48**:2150–2157.
6. Verma S, Mazer CD, Al-Omran M, Inzucchi SE, Fitchett D, Hehnke U, George JT, Zinman B. Cardiovascular outcomes and safety of empagliflozin in patients

- with type 2 diabetes mellitus and peripheral artery disease: a subanalysis of EMPA-REG OUTCOME. *Circulation* 2017; doi: 10.1161/CIRCULATIONAHA.117.032031 [Epub ahead of print].
7. Bonaca MP, Nault P, Giugliano RP, Keech AC, Pineda AL, Kanevsky E, Kuder J, Murphy SA, Jukema JW, Lewis BS, Tokgozoglu L, Somaratne R, Sever PS, Pedersen TR, Sabatine MS. Low-density lipoprotein cholesterol lowering with evolocumab and outcomes in patients with peripheral artery disease: insights from the FOURIER Trial (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk). *Circulation* 2017; doi: 10.1161/CIRCULATIONAHA.117.032235.
 8. Kränkenberg H, Zeller T, Ingwersen M, Schmalstieg J, Gissler HM, Nikol S, Baumgartner I, Diehm N, Nickling E, Müller-Hülsbeck S, Schmiedel R, Torsello G, Hochholzer W, Stelzner C, Brechtel K, Ito W, Kickuth R, Blessing E, Thieme M, Nakonieczny J, Nolte T, Gareis R, Boden H, Sixt S. Self-expanding versus balloon-expandable stents for iliac artery occlusive disease: the randomized ICE trial. *JACC Cardiovasc Interv* 2017; **10**:1694–1704.
 9. Ott I, Cassese S, Groha P, Steppich B, Hadamitzky M, Ibrahim T, Kufner S, Dewitz K, Hiendlmayer R, Laugwitz KL, Schunkert H, Kastrati A, Fusaro M. Randomized comparison of paclitaxel-eluting balloon and stenting versus plain balloon plus stenting versus directional atherectomy for femoral artery disease (ISAR-STATH). *Circulation* 2017; **135**:2218–2226.
 10. Krishnan P, Faries P, Niazi K, Jain A, Sachar R, Bachinsky WB, Cardenas J, Werner M, Brodmann M, Mustapha JA, Mena-Hurtado C, Jaff MR, Holden AH, Lyden SP. Stellarex drug-coated balloon for treatment of femoropopliteal disease: twelve-month outcomes from the randomized ILLUMINATE pivotal and pharmacokinetic studies. *Circulation* 2017; **136**:1102–1113.
 11. Schroeder H, Werner M, Meyer DR, Reimer P, Krüger K, Jaff MR, Brodmann M; ILLUMINATE EU RCT Investigators. Low-dose paclitaxel-coated versus uncoated percutaneous transluminal balloon angioplasty for femoropopliteal peripheral artery disease: one-year results of the ILLUMINATE European Randomized Clinical Trial (Randomized Trial of a Novel Paclitaxel-Coated Percutaneous Angioplasty Balloon). *Circulation* 2017; **135**:2227–2236.
 12. Weitz JI, Lensing AWA, Prins MH, Bauersachs R, Beyer-Westendorf J, Bounameaux H, Brighton TA, Cohen AT, Davidson BL, Decousus H, Freitas MCS, Holberg G, Kakkar AK, Haskell L, van Bellen B, Pap AF, Berkowitz SD, Verhamme P, Wells PS, Prandoni P. Investigators EC. Rivaroxaban or aspirin for extended treatment of venous thromboembolism. *N Engl J Med* 2017; **376**:1211–1222.
 13. Vedantham S, Goldhaber SZ, Julian JA, Kahn SR, Jaff MR, Cohen DJ, Magnuson E, Razavi MK, Comerota AJ, Gornik HL, Murphy TP, Lewis L, Duncan JR, Nieters P, Derfler MC, Filion M, Gu CS, Kee S, Schneider J, Saad N, Blinder M, Moll S, Sacks D, Lin J, Rundback J, Garcia M, Razdan R, VanderWoude E, Marques V, Kearon C. ATTRACT Trial Investigators. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. *N Engl J Med* 2017; **377**:2240–2252.
 14. Verma AA, Masoom H, Rawal S, Guo Y, Razak F. Investigators G. Pulmonary embolism and deep venous thrombosis in patients hospitalized with syncope: a multicenter cross-sectional study in Toronto, Ontario, Canada. *JAMA Intern Med* 2017; **177**:1046–1048.
 15. Darmon A, Bhatt DL, Elbez Y, Aboyans V, Anand S, Bosch J, Branch K, Conolly SJ, Dyal L, Eikelboom JW, Fox KAA, Keltai K, Probstfeld J, Yusuf S, Abtan J, Sorbets E, Eagle KA, Ducrocq G, Steg PG. External applicability of the COMPASS trial: an analysis of the reduction of atherothrombosis for continued health (REACH) registry. *Eur Heart J* 2018; **39**:750–757.
 16. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondur N, Shaw W, Law G, Desai M, Matthews DR. CANVAS Program Collaborative Group. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med* 2017; **377**:644–657.
 17. Freisinger E, Malyar NM, Reinecke H, Lawall H. Impact of diabetes on outcome in critical limb ischemia with tissue loss: a large-scaled routine data analysis. *Cardiovasc Diabetol* 2017; **16**:41.
 18. Kolte D, Kennedy KF, Shishchik MH, Abbott JD, Khera S, Soukas P, Mamdani ST, Hyder ON, Drachman DE, Aronow HD. Thirty-day readmissions after endovascular or surgical therapy for critical limb ischemia: analysis of the 2013 to 2014 nationwide readmissions databases. *Circulation* 2017; **136**:167–176.
 19. Jaff MR, Nelson T, Ferko N, Martinson M, Anderson LH, Hollmann S. Endovascular interventions for femoropopliteal peripheral artery disease: a network meta-analysis of current technologies. *J Vasc Interv Radiol* 2017; **28**:1617–1627.
 20. Smilowitz NR, Gupta N, Guo Y, Berger JS, Bangalore S. Perioperative acute myocardial infarction associated with non-cardiac surgery. *Eur Heart J* 2017; **38**:2409–2417.
 21. Shah Z, Masoomi R, Thapa R, Wani M, Chen J, Dawn B, Rymer M, Gupta K. Optimal medical management reduces risk of disease progression and ischemic events in asymptomatic carotid stenosis patients: a long-term follow-up study. *Cerebrovasc Dis* 2017; **44**:150–159.
 22. Bennett KM, Scarborough JE. Carotid artery stenting is associated with a higher incidence of major adverse clinical events than carotid endarterectomy in female patients. *J Vasc Surg* 2017; **66**:794–801.
 23. Rantner B, Kollerits B, Roubin GS, Rantner B, Kollerits B, Roubin GS, Ringleb PA, Jansen O, Howard G, Hendrikse J, Halliday A, Gregson J, Eckstein HH, Calvet D, Bulbulia R, Bonati LH, Becquemain JP, Algra A, Brown MM, Mas JL, Brott TG, Fraedrich G. Carotid Stenosis Trialists' Collaboration. Early endarterectomy carries a lower procedural risk than early stenting in patients with symptomatic stenosis of the internal carotid artery: results from 4 randomized controlled trials. *Stroke* 2017; **48**:1580–1587.
 24. Knappich C, Kuehn A, Tsantilis P, Schmid S, Breitenkreuz T, Kallmayer M, Zimmermann A, Eckstein HH. The use of embolic protection devices is associated with a lower stroke and death rate after carotid stenting. *JACC Cardiovasc Interv* 2017; **10**:1257–1265.
 25. Venermo M, Wang G, Sedrakyan A, Mao J, Eldrup N, DeMartino R, Mani K, Altreuther M, Beiles B, Menyhei G, Danielsson G, Thomson I, Heller G, Setacci C, Björck M, Cronenwett J. Editor's choice - carotid stenosis treatment: variation in international practice patterns. *Eur J Vasc Endovasc Surg* 2017; **53**:511–519.
 26. Saura D, Dulgheru R, Caballero L, Bernard A, Kou S, Gonjilashvili N, Athanassopoulos GD, Barone D, Baroni M, Cardim N, Hagendorff A, Hristova K, Lopez T, de la Morena G, Popescu BA, Penicka M, Ozyigit T, Rodrigo Carbonero JD, Van De Veire N, Von Bardeleben RS, Vinereanu D, Zamorano JL, Gori AS, Cosyns B, Donal E, Habib G, Addetia K, Lang RM, Badano LP, Lancellotti P. Two-dimensional transthoracic echocardiographic normal reference ranges for proximal aorta dimensions: results from the EACVI NORRE study. *Eur Heart J Cardiovasc Imaging* 2017; **18**:167–179.
 27. Thomas IC, McClelland RL, Michos ED, Allison MA, Forbang NI, Longstreth WT, Jr, Post WS, Wong ND, Budoff MJ, Criqui MH. Density of calcium in the ascending thoracic aorta and risk of incident cardiovascular disease events. *Atherosclerosis* 2017; **265**:190–196.
 28. Kim J, Budoff MJ, Nasir K, Wong ND, Yeboah J, Al-Mallah MH, Shea S, Dardari ZA, Blumenthal RS, Blaha MJ, Cainzos-Achirica M. Thoracic aortic calcium, cardiovascular disease events, and all-cause mortality in asymptomatic individuals with zero coronary calcium: the Multi-Ethnic Study of Atherosclerosis (MESA). *Atherosclerosis* 2017; **257**:1–8.
 29. Ohshima Y, Ambale-Venkatesh B, Noda C, Kim JY, Tanami Y, Teixeira-Tura G, Chugh AR, Redheuil A, Liu CY, Wu CO, Hundley WG, Bluemke DA, Guller E, Lima JAC. Aortic arch pulse wave velocity assessed by magnetic resonance imaging as a predictor of incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis). *Hypertension* 2017; **70**:524–530.
 30. Lescan M, Veseli K, Oikonomou A, Walker T, Lausberg H, Blumenstock G, Bamberg F, Schlensak C, Krüger T. Aortic elongation and Stanford B dissection: the Tübingen Aortic Pathoanatomy (TAIPAN) Project. *Eur J Vasc Endovasc Surg* 2017; **54**:164–169.
 31. Craiem D, El Batti S, Casciaro ME, Mousseaux E, Sirieix ME, Simon A, Alsac JM. Age-related changes of thoracic aorta geometry used to predict the risk for acute type B dissection. *Int J Cardiol* 2017; **228**:654–660.
 32. Ghulam QM1, Bredahl KK2, Lönn L, Rouet L, Sillesen HH5. Eiberg JP6: follow-up on small abdominal aortic aneurysms using three dimensional ultrasound: volume versus diameter. *Eur J Vasc Endovasc Surg* 2017; **54**:439–445.
 33. Laine MT, Laukontaus SJ, Sund R, Aho PS, Kantonen I, Alback A, Venermo M. A population-based study of abdominal aortic aneurysm treatment in Finland 2000 to 2014. *Circulation* 2017; **136**:1726–1734.
 34. Budtz-Lilly J, Venermo M, Debus S, Behrendt CA, Altreuther M, Beiles B, Szeberin Z, Eldrup N, Danielsson G, Thomson I, Wigger P, Björck M, Loftus I, Mani K. Assessment of international outcomes of intact abdominal aortic aneurysm repair over 9 years. *Eur J Vasc Endovasc Surg* 2017; **54**:13–20.
 35. Tomee SM, Bastiaannet E, Schermerhorn ML, Golledge J, Hamming JF, Lindeman JH. The consequences of real life practice of early abdominal aortic aneurysm repair: a cost-benefit analysis. *Eur J Vasc Endovasc Surg* 2017; **54**:28–33.
 36. Abrahá I, Luchetta ML, De Florio R, Cozzolino F, Casazza G, Duca P, Parente B, Orso M, Germani A, Eusebi P, Montedori A. Ultrasonography for endoleak detection after endoluminal abdominal aortic aneurysm repair. *Cochrane Database Syst Rev* 2017; **6**:CD010296.
 37. Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, Bauersachs R, Brekelmans MP, Büller HR, Elias A, Farge D, Konstantinides S, Palareti G, Prandoni P, Righini M, Torbicki A, Vlachopoulos C, Brodmann M. Diagnosis and management of acute deep vein thrombosis: a joint consensus document from the European society of cardiology working groups of aorta and peripheral circulation and pulmonary circulation and right ventricular function. *Eur Heart J* 2017; doi: 10.1093/eurheartj/ehx003.
 38. Prandoni P, Vedovetto V, Ciammaichella M, Bucherini E, Corradini S, Enea I, Cosmi B, Mumoli N, Visona A, Barillari G, Bova C, Quintavalla R, Zanatta N, Pedrini S, Villalta S, Camporese G, Testa S, Parisi R, Becattini C, Cuppini S, Pengo V, Palareti G, Morgagni I. Residual vein thrombosis and serial D-dimer for

- the long-term management of patients with deep venous thrombosis. *Thromb Res* 2017;**154**:35–41.
39. De Carlo M, Mazzolai L, Bossone E, Brodmann M, Micari A, Muiesan ML, Riccio JB, Stabile E, Agnelli G, Aboyans V. ESC Working Group on Aorta and Peripheral Vascular Diseases. The year in cardiology 2016: peripheral circulation. *Eur Heart J* 2017;**38**:1028–1033.
 40. Rodger MA, Le Gal G, Anderson DR, Schmidt J, Pernod G, Kahn SR, Righini M, Mismetti P, Kearon C, Meyer G, Elias A, Ramsay T, Ortel TL, Huisman MV, Kovacs MJ. Investigators RIS. Validating the HERDOO2 rule to guide treatment duration for women with unprovoked venous thrombosis: multinational prospective cohort management study. *BMJ* 2017;**356**:j1065.
 41. Prandoni P, Ageno W, Mumoli N, Zanatta N, Imberti D, Visonà A, Ciammaichella M, Simioni L, Cappelli R, Bucherini E, Di Nisio M, Avruscio G, Camporese G, Parisi R, Cuppini S, Turatti G, Noventa F, Sarolo L. Recanalization rate in patients with proximal vein thrombosis treated with the direct oral anticoagulants. *Thromb Res* 2017;**153**:97–100.
 42. Haig Y, Enden T, Grøtta O, Kløw NE, Slagsvold CE, Ghanima W, Sandvik L, Hafsahl G, Holme PA, Holmen LO, Njaaastad AM, Sandbæk G, Sandset PM. CaVenT Study Group. Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomized controlled trial. *Lancet Haematol* 2016;**3**:e64–e71.
 43. van Es N, Di Nisio M, Cesarman G, Kleinjan A, Otten H-M, Mahé I, Wilts IT, Twint DC, Porreca E, Arrieta O, Stépanian A, Smit K, De Tursi M, Bleker SM, Bossuyt PM, Nieuwland R, Kamphuisen PW, Büller HR. Comparison of risk prediction scores for venous thromboembolism in cancer patients: a prospective cohort study. *Haematologica* 2017;**102**:1494–1501.
 44. Alatri A, Mazzolai L, Font C, Tafur A, Valle R, Marchena PJ, Ballaz A, Tiraferri E, Font L, Monreal M, Riete Investigators T. Low discriminating power of the modified Ottawa VTE risk score in a cohort of patients with cancer from the RIETE Registry. *Thromb Haemost* 2017;**117**:1630–1636.
 45. Alatri A, Mazzolai L, Kucher N, Aujesky D, Beer JH, Baldi T, Banyai M, Hayoz D, Kaeslin T, Korte W, Escher R, Husmann M, Frauchiger B, Engelberger RP, Baumgartner I, Spirk D. The Modified Ottawa Score and Clinical Events in Hospitalized Patients with Cancer-Associated Thrombosis from the Swiss VTE Registry. *Semin Thromb Hemost* 2017;**43**:871–876.
 46. van der Hulle T, Cheung WY, Kooij S, Beenen LFM, van Bommel T, van Es J, Faber LM, Hazelaar GM, Heringhaus C, Hofstee H, Hovens MMC, Kaasjager KAH, van Klink RCJ, Kruip MJHA, Loeffen RF, Mairuhu ATA, Middeldorp S, Nijkeuter M, van der Pol LM, Schol-Gelok S, ten Wolde M, Klok FA, Huisman MV, Fogteloo AJ, Kroft LJM, Brekelmans MP, Vermaire RMJ, Bastiaansen-Bergsma H, Biedermann JS, Klijn A, van der Voort S, Lieveld AWE, de Jong PY, Schaar CG, del Sol AI. group Ys. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. *Lancet* 2017;**390**:289–297.
 47. Robert-Ebadi H, Glauser F, Planquette B, Mounneh T, Le Gal G, Righini M. Safety of multidetector computed tomography pulmonary angiography to exclude pulmonary embolism in patients with a likely pretest clinical probability. *J Thromb Haemost* 2017;**15**:1584–1590.
 48. Oqab Z, Ganshorn H, Sheldon R. Prevalence of pulmonary embolism in patients presenting with syncope. A systematic review and meta-analysis. *Am J Emerg Med* 2017; doi:10.1016/j.ajem.2017.09.015.
 49. Frizell A, Fogel N, Steenblik J, Carlson M, Bledsoe J, Madsen T. Prevalence of pulmonary embolism in patients presenting to the emergency department with syncope. *Am J Emerg Med* 2017; doi:10.1016/j.ajem.2017.07.090.
 50. Konstantinides SV, Vicaut E, Danays T, Becattini C, Bertolotti L, Beyer-Westendorf J, Bouvaist H, Couturaud F, Dellas C, Duerschmied D, Empen K, Ferrari E, Galie N, Jimenez D, Kostrubiec M, Kozak M, Kupatt C, Lang IM, Lankeit M, Meneveau N, Palazzini M, Pruszczyk P, Rugolotto M, Salvi A, Sanchez O, Schellong S, Sobkowicz B, Meyer G. Impact of thrombolytic therapy on the long-term outcome of intermediate-risk pulmonary embolism. *J Am Coll Cardiol* 2017;**69**:1536–1544.